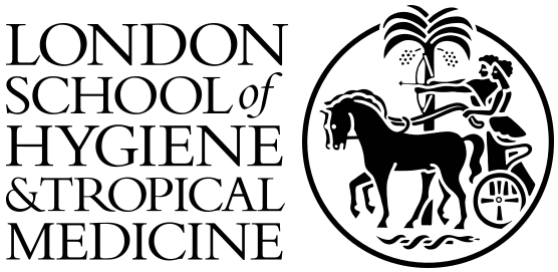

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Short Communication

Estimating the annual risk of HIV transmission within HIV sero-discordant couples in sub-Saharan Africa

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ABSTRACT

Objective: To estimate the annual risk of HIV transmission (ϕ) within HIV sero-discordant couples in 23 countries in sub-Saharan Africa (SSA), by utilizing newly available national population-based data and accounting for factors known to potentially affect this estimation.
Methods: We used a recently developed pair-based mathematical model that accommodates for HIV-dynamics temporal variation, sexual risk-behavior heterogeneity, and antiretroviral therapy (ART) scale-up.
Results: Estimated country-specific ϕ (in absence of ART) ranged between 4.2% (95% uncertainty interval (UI): 1.9%-6.3%) and 47.4% (95% UI: 37.2%-69.0%) per person-year (ppy), with a median of 12.4%. ϕ was strongly associated with HIV prevalence, with a Pearson correlation coefficient of 0.92, and was larger in high- versus low-HIV-prevalence countries. ϕ increased by 1.31% (95% confidence interval: 1.00%-1.55%) ppy for every 1% increase in HIV prevalence.
Conclusions: ϕ estimates were similar to earlier estimates, and suggested considerable heterogeneity in HIV infectiousness across SSA. This heterogeneity may explain, partly, the differences in epidemic scales.

Introduction

Quantifying the annual risk of HIV transmission (ϕ) within HIV sero-discordant couples (SDCs) in sub-Saharan Africa (SSA) is critical to understanding HIV epidemiology and implementation of intervention programs. Previously, we estimated ϕ and its variation and found that it varies across countries (Chemaitelly et al., 2014). We also found that ϕ is within the range, but overall higher, than that estimated in setting-specific longitudinal studies following cohorts of SDCs in Africa (Chemaitelly et al., 2014).

A key limitation in earlier estimates is that the modeling approach did not factor the temporal variation in HIV prevalence, sexual risk-behavior heterogeneity, and scale-up of antiretroviral therapy (ART). Although the spatial dimension does not appear to play a critical role in sero-discordancy dynamics (Cuadros and Abu-Raddad, 2016), historical and future patterns of sero-discordancy were found dependent on the temporal changes in HIV epidemics (Awad et al., 2017).

We present here new estimates for ϕ in 23 SSA countries using an elaborate modeling approach that accommodates for epidemic temporal variation, sexual risk-behavior heterogeneity, and ART scale-up. The new estimates also utilize all rounds of the nationally representative household surveys, the Demographic and Health Surveys (DHS) (MEASURE DHS, 2017), for each country in SSA up to 2015.

Methods

A pair-based model was used to estimate the mean ϕ over the duration of the modeled epidemics. Briefly, the model consists of a set of coupled nonlinear differential equations stratifying the population according to stable-couple status, risk-behavior group, HIV status, and ART-treatment status (Awad et al., 2017). The model accommodated for epidemic temporal variation, in its different phases, and for the risk of acquiring the infection from other non-stable partners (i.e. through extramarital sex). Ten risk groups, a sexual-risk mixing matrix, and temporal changes in risk behavior were also incorporated to account for heterogeneity and

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declines in risk of HIV exposure (Awad et al., 2017; Awad and Abu-Raddad, 2014). The country-specific ART coverage was set as reported (UNAIDS, 2015b), and ART reduced the overall HIV infectiousness (by 96% (Cohen et al., 2011)) and slowed disease progression (Awad et al., 2017).

Countries were included based on availability of DHS sero-prevalence surveys to apply the model to these data (MEASURE DHS, 2017). The model was parameterized using natural history and epidemiology data from SSA (Awad et al., 2017). We estimated ϕ by fitting the country-specific 1990-2015 HIV prevalence and sero-discordancy measures (MEASURE DHS, 2017; Chemaitelly et al., 2012). All measures were weighted equally in the fitting. Multivariate uncertainty analysis was conducted for the model structural parameters, and the country-specific ϕ mean and 95% uncertainty interval (UI) were estimated using a log-normal fit. Association between the country-specific HIV prevalence and estimated ϕ was assessed using linear regression.

Further details about this model and its parameterization can be found elsewhere (Awad et al., 2017).

Results

Table S1 in the online version, at DOI:10.1016/j.ijid.2017.10.022, shows the derived DHS HIV prevalence and sero-discordancy measures that were fitted using the model. Estimated country-specific ϕ (in absence of ART) ranged between 4.2% (95% UI: 1.9%-6.3%) and 47.4% (95% UI: 37.2%-69.0%) per person-year (ppy), with a median of 12.4% ppy (Figure 1). The median was 9.4% ppy in low-HIV-prevalence countries (HIV prevalence $\leq$5%) and 25.2% ppy in high-HIV-prevalence countries (HIV prevalence >5%).

Figure 2 illustrates the association between the estimated ϕ and HIV prevalence in 2015, with Burundi and Rwanda excluded as outliers. ϕ was strongly correlated with HIV prevalence—Pearson correlation coefficient of 0.92 with HIV prevalence explaining 85% of the variation. ϕ increased by 1.31% (95% confidence interval: 1.00%-1.55%) ppy for every 1% increase in HIV prevalence (p-value < 0.001). The correlation was also assessed with HIV prevalence in earlier years, to capture the correlation at different epidemic phases. The correlation coefficient increased steadily with year, and was strong for all years starting from the mid-1990s. For example, the correlation coefficient was 0.88 with HIV prevalence in 2000, thereby explaining 77% of the variation.

Discussion

We presented new estimates of HIV infectiousness within SDCs in 23 SSA countries. Despite the new analytical approach and updated input data, ϕ estimates were similar to those estimated earlier (Figure 1; p-value for difference in overall mean = 0.71) (Chemaitelly et al., 2014). The estimated ϕ values indicated also large variability in infectiousness across countries. The contrasting HIV epidemic trajectories in SSA are possibly a consequence of the variability in ϕ—HIV prevalence in different epidemic phases was strongly associated with HIV infectiousness (Figure 2). This highlights how ϕ is high and needs to be addressed in high HIV prevalence countries, such as in Swaziland with a ϕ of 47% ppy and HIV prevalence of 29%. As more quality population-based data become available over the coming years, it will be useful to update these estimates based on more comprehensive data from more survey rounds.

Our estimates for ϕ are roughly within the range of estimates from longitudinal studies, of 1.2%-22.0% ppy (Chemaitelly et al., 2014)—but higher on average. The lower observed ϕ in longitutal studies may be explained by known biases, such as higher levels of

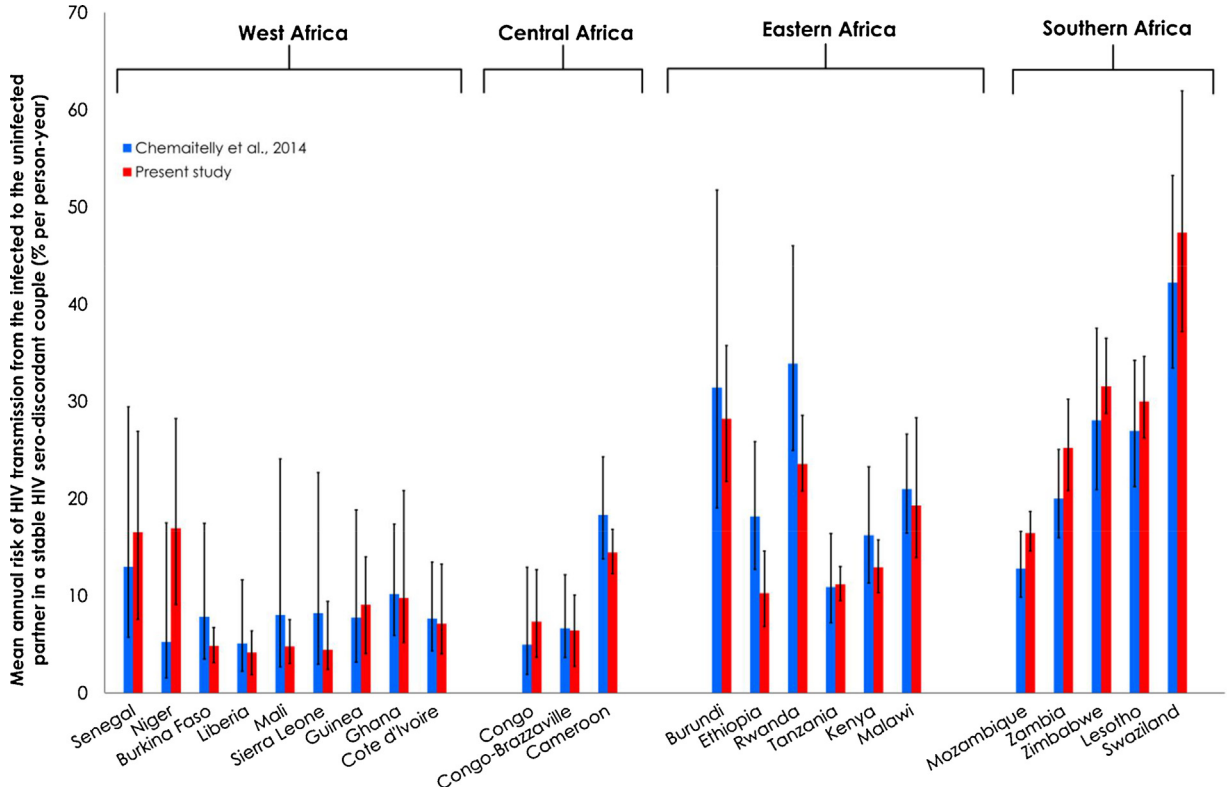

Figure 1. Mean and 95% uncertainty interval for the country-specific annual risk of HIV transmission (ϕ) from the infected to the uninfected partner in a stable HIV sero-discordant couple across sub-Saharan Africa. The blue bars indicate the predictions of Chemaitelly et al. (2014), while the red bars indicate the predictions of the present study. Countries are shown by sub-region (UNICEF, 2008) and in order of increasing 2015 HIV prevalence. HIV prevalence in 2015 is based on UNAIDS estimates (UNAIDS, 2015a).

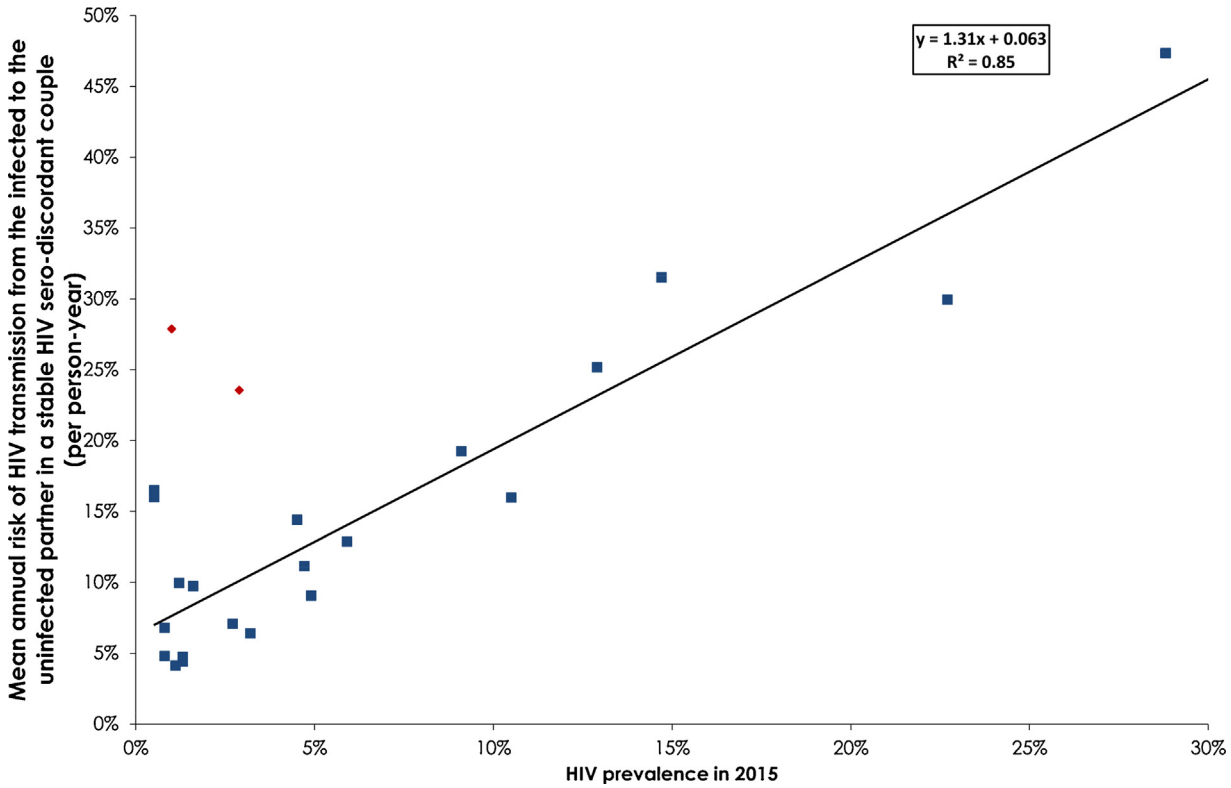

Figure 2. The variation in the mean annual risk of HIV transmission (ϕ) from the infected to the uninfected partner in a stable HIV sero-discordant couple with respect to HIV prevalence in the population. Country-specific estimates marked in red are excluded from the analysis as outliers. HIV prevalence in 2015 is based on UNAIDS estimates (UNAIDS, 2015a).

sero-status disclosure and intense counseling, in the studied cohorts versus the population at large, as well as selection bias of more "resistant" and "surviving" couples in the recruitment of SDCs (Chemaitelly et al., 2014).

The observed variability in ϕ across countries is supported by a body of evidence indicating a role for biological cofactors in HIV transmission such as male circumcision (Weiss et al., 2008), co-infections (whether sexually transmitted or not) (Korenromp et al., 2001; Abu-Raddad et al., 2006; Abu-Raddad et al., 2012), variation in the susceptibility to HIV (Nagelkerke et al., 2009; Kaul et al., 2011), virus sub-type (Novitsky et al., 2011), and hormonal contraception use (Heffron et al., 2012). Behavioral factors may also play a role such as variations in uptake of condom use (Hughes et al., 2012) and coital frequency (Brown, 2000). While our study estimated the overall mean ϕ across epidemic evolution, it would be of interest in future studies to investigate how these multiple cofactors could have affected ϕ's variation across countries and over time.

Our study has limitations. We assumed a specific level of sexual mixing between risk groups based on earlier work (Abu-Raddad and Longini, 2008), but this assumption had no impact on the estimated ϕ, as demonstrated in a sensitivity analysis (Figure S1 in the online version, at DOI:10.1016/j.ijid.2017.10.022). We assumed that ϕ was constant during the observed time frame (1980-2030), but prevalence of cofactors affecting ϕ, such as male circumcision, may have changed over time—the estimated ϕ is simply an overall average over the modeled epidemic duration. Burundi and Rwanda were excluded from the regression analysis because of very high ϕ relative to HIV prevalence—possibly because of too small and non-representative SDC datasets.

In summary, HIV infectiousness within sexual partnerships appears to vary by country probably due to a combination of biological and behavioral cofactors. This heterogeneity may explain, partly, the differences in the scales of SSA epidemics. This cumulative and consistent evidence for heterogeneity in infectiousness may underline a hallmark of the epidemiology of HIV—the extensive geographical variability in transmission patterns in comparison to other infections.

Contributors

SFA co-designed and programmed the model, conducted the modeling analyses, and wrote the first draft of the article. HC managed the Demographic and Health Surveys databases and conducted the statistical analyses on these databases. LJA conceived and led the design of the study and model, analyses, and drafting of the article. All authors contributed to the interpretation of the results and writing of the article.

Competing interests

We declare that we have no conflict of interest to disclose.

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